10/524,517

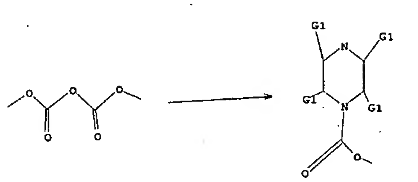
[redacted]

1 hit

```
Connecting via Winsock to STN


Welcome to STN International!  Enter x:x

LOGINID:SSPTAEAL1624

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * *     Welcome to STN International     * * * * * * * * *

 NEWS  1           Web Page for STN Seminar Schedule - N. America
 NEWS  2  MAR 15   WPIDS/WPIX enhanced with new FRAGHITSTR display format
 NEWS  3  MAR 16   CASREACT coverage extended
 NEWS  4  MAR 20   MARPAT now updated daily
 NEWS  5  MAR 22   LWPI reloaded
 NEWS  6  MAR 30   RDISCLOSURE reloaded with enhancements
 NEWS  7  APR 02   JICST-EPLUS removed from database clusters and STN
 NEWS  8  APR 30   GENBANK reloaded and enhanced with Genome Project ID field
 NEWS  9  APR 30   CHEMCATS enhanced with 1.2 million new records
 NEWS 10  APR 30   CA/CAplus enhanced with 1870-1889 U.S. patent records
 NEWS 11  APR 30   INPADOC replaced by INPADOCDB on STN
 NEWS 12  MAY 01   New CAS web site launched
 NEWS 13  MAY 08   CA/CAplus Indian patent publication number format defined
 NEWS 14  MAY 14   RDISCLOSURE on STN Easy enhanced with new search and display
                   fields
 NEWS 15  MAY 21   BIOSIS reloaded and enhanced with archival data
 NEWS 16  MAY 21   TOXCENTER enhanced with BIOSIS reload
 NEWS 17  MAY 21   CA/CAplus enhanced with additional kind codes for German
                   patents
 NEWS 18  MAY 22   CA/CAplus enhanced with IPC reclassification in Japanese
                   patents
 NEWS 19  JUN 27   CA/CAplus enhanced with pre-1967 CAS Registry Numbers
 NEWS 20  JUN 29   STN Viewer now available
 NEWS 21  JUN 29   STN Express, Version 8.2, now available
 NEWS 22  JUL 02   LEMBASE coverage updated
 NEWS 23  JUL 02   LMEDLINE coverage updated
 NEWS 24  JUL 02   SCISEARCH enhanced with complete author names
 NEWS 25  JUL 02   CHEMCATS accession numbers revised
 NEWS 26  JUL 02   CA/CAplus enhanced with utility model patents from China
 NEWS 27  JUL 16   CAplus enhanced with French and German abstracts
 NEWS 28  JUL 18   CA/CAplus patent coverage enhanced

 NEWS EXPRESS  29 JUNE 2007:  CURRENT WINDOWS VERSION IS V8.2,
               CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 05 JULY 2007.

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that
specific topic.
```



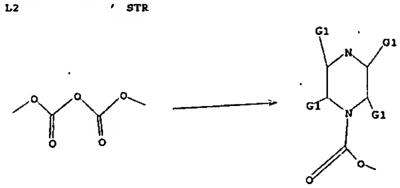
```
  All use of STN is subject to the provisions of the STN Customer
  agreement.  Please note that this agreement limits use to scientific
  research.  Use for software development or design or implementation
  of commercial gateways or other similar uses is prohibited and may
  result in loss of user privileges and other penalties.

* * * * * * * * * * * * * *  STN Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 17:11:43 ON 24 JUL 2007

=> file reg
COST IN U.S. DOLLARS                              SINCE FILE     TOTAL
                                                       ENTRY   SESSION
FULL ESTIMATED COST                                     0.21      0.21

FILE 'REGISTRY' ENTERED AT 17:11:49 ON 24 JUL 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:    23 JUL 2007  HIGHEST RN 943188-87-2
DICTIONARY FILE UPDATES:   23 JUL 2007  HIGHEST RN 943188-87-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10524517casreact.str

L1       STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1                STR
```


```
G1 C,H,O,X


Structure attributes must be viewed using STN Express query preparation.


=> s l1 full
MULTIPLE ROLE QUERIES ARE NOT ALLOWED IN A NON-REACTION FILE

=> s l1
MULTIPLE ROLE QUERIES ARE NOT ALLOWED IN A NON-REACTION FILE

=> file reg
COST IN U.S. DOLLARS                              SINCE FILE     TOTAL
                                                       ENTRY   SESSION
FULL ESTIMATED COST                                     0.90      1.11

FILE 'REGISTRY' ENTERED AT 17:12:55 ON 24 JUL 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:    23 JUL 2007  HIGHEST RN 943188-87-2
DICTIONARY FILE UPDATES:   23 JUL 2007  HIGHEST RN 943188-87-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10524517casreact.str
```

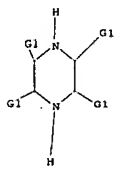


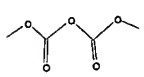
```
L2       STRUCTURE UPLOADED

=> d l2
L2 HAS NO ANSWERS
L2                STR
```

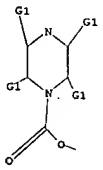



```
G1 C,H,O,X


Structure attributes must be viewed using STN Express query preparation.


=> file casreact
COST IN U.S. DOLLARS                              SINCE FILE     TOTAL
                                                       ENTRY   SESSION
FULL ESTIMATED COST                                     0.45      1.56

FILE 'CASREACT' ENTERED AT 17:13:29 ON 24 JUL 2007
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.

FILE CONTENT:1840 - 21 Jul 2007 VOL 147 ISS 5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

***********************************************************
*                                                         *
*     CASREACT now has more than 12 million reactions     *
*                                                         *
***********************************************************

Some CASREACT records are derived from the ZIC/VINITI database (1974-1999)
provided by InfoChem, INPI data prior to 1986, and Biotransformations
database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance
identification.

=> s l2
SAMPLE SEARCH INITIATED 17:13:34 FILE 'CASREACT'
SCREENING COMPLETE -      220 REACTIONS TO VERIFY FROM       22 DOCUMENTS
```

```
100.0% DONE     220 VERIFIED      31 HIT RXNS                    5 DOCS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:   ONLINE  **COMPLETE**
                         BATCH   **COMPLETE**
PROJECTED VERIFICATIONS:        3511 TO     5289
PROJECTED ANSWERS:                 5 TO      234

L3             5 SEA SSS SAM L2 (    31 REACTIONS)

=> s l2 full
FULL SEARCH INITIATED 17:13:39 FILE 'CASREACT'
SCREENING COMPLETE -     6689 REACTIONS TO VERIFY FROM      449 DOCUMENTS

100.0% DONE    6689 VERIFIED     1173 HIT RXNS                 128 DOCS
SEARCH TIME: 00.00.02

L4           128 SEA SSS FUL L2 (  1173 REACTIONS)

=>
Uploading C:\Program Files\Stnexp\Queries\10524517reagents.str

L5      STRUCTURE UPLOADED

=> d l5
L5 HAS NO ANSWERS
L5              STR
```








```
G1 C,H,O,X
```



```
Structure attributes must be viewed using STN Express query preparation.

=> s l5
SAMPLE SEARCH INITIATED 17:20:13 FILE 'CASREACT'
SCREENING COMPLETE -      100 REACTIONS TO VERIFY FROM       14 DOCUMENTS

100.0% DONE     100 VERIFIED      19 HIT RXNS                    4 DOCS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:   ONLINE  **COMPLETE**
                         BATCH   **COMPLETE**
PROJECTED VERIFICATIONS:       1401 TO     2599
PROJECTED ANSWERS:                4 TO      199

L6             4 SEA SSS SAM L5 (    19 REACTIONS)

=> s l5 full
FULL SEARCH INITIATED 17:20:18 FILE 'CASREACT'
SCREENING COMPLETE -     3730 REACTIONS TO VERIFY FROM      350 DOCUMENTS

100.0% DONE    3730 VERIFIED     401 HIT RXNS                  63 DOCS
SEARCH TIME: 00.00.01

L7            63 SEA SSS FUL L5 (   401 REACTIONS)

=> file casreact
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY     SESSION
FULL ESTIMATED COST                             231.60      233.16

FILE 'CASREACT' ENTERED AT 17:20:23 ON 24 JUL 2007
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.

FILE CONTENT:1840 - 21 Jul 2007 VOL 147 ISS 5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

**********************************************************
*                                                        *
*     CASREACT now has more than 12 million reactions    *
*                                                        *
**********************************************************

Some CASREACT records are derived from the ZIC/VINITI database (1974-1999)
provided by InfoChem, INPI data prior to 1986, and Biotransformations
database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance
identification.

=> s l7 full
```



```
FULL SEARCH INITIATED 17:20:33 FILE 'CASREACT'
SCREENING COMPLETE -     3730 REACTIONS TO VERIFY FROM      350 DOCUMENTS

100.0% DONE    3730 VERIFIED     401 HIT RXNS                  63 DOCS
SEARCH TIME: 00.00.01

L8            63 SEA SSS FUL L5 (   401 REACTIONS)

=> s l8 and py<2003
        486823 PY<2003
L9             21 L8 AND PY<2003

=> d ibib abs hitstr tot
'HITSTR' IS NOT A VALID FORMAT FOR FILE 'CASREACT'

The following are valid formats:

ABS -------- GI and AB
ALL -------- BIB, AB, IND, RE, Single-step Reactions
APPS ------- AI, PRAI
BIB -------- AN, plus Bibliographic Data
CAN -------- List of CA abstract numbers without answer numbers
CBIB ------- AN, plus Compressed Bibliographic Data
DALL ------- ALL, delimited (end of each field identified)
IABS ------- ABS, indented with text labels
IALL ------- ALL, indented with text labels
IBIB ------- BIB, indented with text labels
IND -------- Indexing data
IPC -------- International Patent Classifications
ISTD ------- STD, indented with text labels
OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

MAX -------- Same as ALL
PATS ------- PI, SO
SCAN ------- TI and FCRD (random display, no answer number.  SCAN
             must be entered on the same line as DISPLAY, e.g.,
             D SCAN.)
SSRX ------- Single-Step Reactions (Map, Diagram, and Summary for
             all single-step reactions)
STD -------- BIB, IPC, and NCL

CRD -------- Compact Display of All Hit Reactions
CRDREF ----- Compact Reaction Display and SO, PY for Reference
FHIT ------- Reaction Map, Diagram, and Summary for first
             hit reaction
FHITCBIB --- FHIT, AN plus CBIB
FCRD ------- First hit in Compact Reaction Display (CRD) format
FCRDREF ---- First hit in Compact Reaction Display (CRD) format with
             CA reference information (SO, PY).  (Default)
FPATH ------ PATH, plus Reaction Summary for the "long path"
FSPATH ----- SPATH, plus Reaction Summary for the "short path"
HIT -------- Reaction Map, Reaction Diagram, and Reaction
             Summary for all hit reactions and fields containing
             hit terms
OCC -------- All hit fields and the number of occurrences of the
```



```
             hit terms in each field.  Includes total number of
             HIT, PATH, SPATH reactions. Labels reactions that have
             incomplete verifications.
PATH ------- Reaction Map and Reaction Diagram for the "long
             path".  Displays all hit reactions, except those
             whose steps are totally included within another hit
             reaction which is displayed
RX --------- Hit Reactions (Map, Diagram, Summary for all hit reactions)
RXG -------- Hit Reaction Graphics (Map and Diagram for all hit reactions)
RXL -------- Hit Reaction Long (Map, Diagram, Summary for all hit reactions)
RXS -------- Hit Reaction Summariers (Map and Summary for all hit reactions)
SPATH ------ Reaction Map and Reaction Diagram for the "short
             path".  Displays all single step reactions which
             contain a hit substance.  Also displays those
             multistep reactions that have a hit substance in both
             the first and last steps of the reaction, except for
             those hit reactions whose steps are totally included
             within another hit reaction which is displayed

To display a particular field or fields, enter the display field
codes.  For a list of the display field codes, enter HELP DFIELDS
at an arrow prompt (=>).  Examples of combinations include: D TI;
D BIB RX; D TI, AU, FCRD.  The information is displayed in the same order
as the specification.  All of the formats, except CRD, CRDREF, FHIT, PATH,
FPATH, SPATH, FSPATH, FCRD, FCRDREF, HIT, RX, RXG, RXS, SCAN, and OCC, may
be used with the DISPLAY command to display the record for a specified
Accession Number.

ENTER DISPLAY FORMAT (FCRDREF):d ibib abs fhit
'D' IS NOT A VALID FORMAT FOR FILE 'CASREACT'

The following are valid formats:

ABS -------- GI and AB
ALL -------- BIB, AB, IND, RE, Single-step Reactions
APPS ------- AI, PRAI
BIB -------- AN, plus Bibliographic Data
CAN -------- List of CA abstract numbers without answer numbers
CBIB ------- AN, plus Compressed Bibliographic Data
DALL ------- ALL, delimited (end of each field identified)
IABS ------- ABS, indented with text labels
IALL ------- ALL, indented with text labels
IBIB ------- BIB, indented with text labels
IND -------- Indexing data
IPC -------- International Patent Classifications
ISTD ------- STD, indented with text labels
OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

MAX -------- Same as ALL.
PATS ------- PI, SO
SCAN ------- TI and FCRD (random display, no answer number.  SCAN
             must be entered on the same line as DISPLAY, e.g.,
             D SCAN.)
SSRX ------- Single-Step Reactions (Map, Diagram, and Summary for
             all single-step reactions)
```

STD -------- BIB, IPC, and NCL

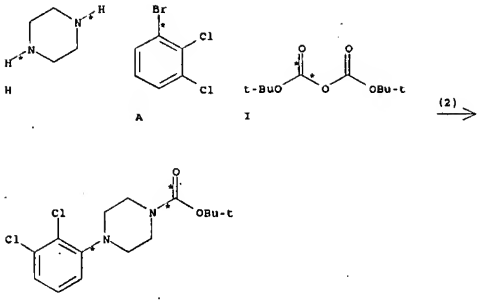
CRD -------- Compact Display of All Hit Reactions
CRDREF ----- Compact Reaction Display and SO, PY for Reference
FHIT ------- Reaction Map, Diagram, and Summary for first hit reaction
FHITCBIB --- FHIT, AN plus CBIB
FCRD ------- First hit in Compact Reaction Display (CRD) format
FCRDREF ---- First hit in Compact Reaction Display (CRD) format with CA reference information (SO, PY). (Default)
FPATH ------ PATH, plus Reaction Summary for the "long path"
FSPATH ----- SPATH, plus Reaction Summary for the "short path"
HIT -------- Reaction Map, Reaction Diagram, and Reaction Summary for all hit reactions and fields containing hit terms
OCC -------- All hit fields and the number of occurrences of the hit terms in each field. Includes total number of HIT, PATH, SPATH reactions. Labels reactions that have incomplete verifications.
PATH ------- Reaction Map and Reaction Diagram for the "long path". Displays all hit reactions, except those whose steps are totally included within another hit reaction which is displayed
RX --------- Hit Reactions. (Map, Diagram, Summary for all hit reactions)
RXG -------- Hit Reaction Graphics (Map and Diagram for all hit reactions)
RXL -------- Hit Reaction Long (Map, Diagram, Summary for all hit reactions)
RXS -------- Hit Reaction Summariers (Map and Summary for all hit reactions)
SPATH ------ Reaction Map and Reaction Diagram for the "short path". Displays all single step reactions which contain a hit substance. Also displays those multistep reactions that have a hit substance in both the first and last steps of the reaction, except for those hit reactions whose steps are totally included within another hit reaction which is displayed

To display a particular field or fields, enter the display field codes. For a list of the display field codes, enter HELP DFIELDS at an arrow prompt (=>). Examples of combinations include: D TI; D BIB RX; D TI, AU, FCRD. The information is displayed in the same order as the specification. All of the formats, except CRD, CRDREF, FHIT, PATH, FPATH, SPATH, FSPATH, FCRD, FCRDREF, HIT, RX, RXG, RXS, SCAN, and OCC, may be used with the DISPLAY command to display the record for a specified Accession Number.

ENTER DISPLAY FORMAT (FCRDREF):fhit

L9 ANSWER 1 OF 21 CASREACT COPYRIGHT 2007 ACS on STN

RX(2) OF 3 H + A + I ===> C



YIELD 75%

RX(2) RCT H 110-85-0, A 56961-77-4

STAGE(1)
SOL 108-88-3 PhMe
CON 10 minutes, 40 deg C

STAGE(2)
CAT 98327-87-8 Phosphine, 1,1'-[1,1'-binaphthalene]-2,2'-diylbis[1,1-diphenyl-, 51364-51-3 Ph2-pentadienone Pd

STAGE(3)
RGT J 6674-22-2 DBU
CON 5 minutes, 60 - 70 deg C

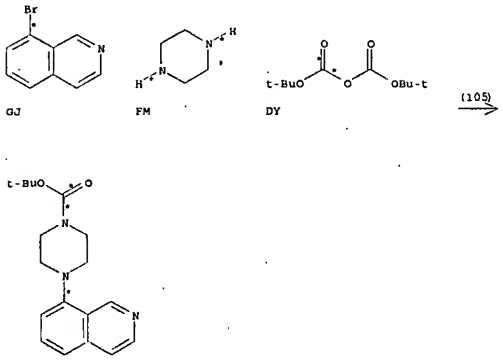
STAGE(4)
RGT K 865-48-5 NaOBu-t
CON 1 - 4 hour

STAGE(5)
RCT I 24424-99-5

PRO C 503315-03-5
NTE yield depends on cat. and base

L9 ANSWER 2 OF 21 CASREACT COPYRIGHT 2007 ACS on STN

RX(105) OF 794 GJ + FM + DY ===> GK...



YIELD 83%

RX(105) RCT GJ 63927-22-0, FM 110-85-0

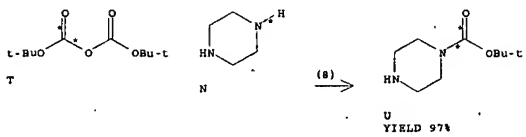
STAGE(1)
RGT BF 865-48-5 NaOBu-t
CAT 51364-51-3 Ph2-pentadienone Pd, 98327-87-8 Phosphine, 1,1'-[1,1'-binaphthalene]-2,2'-diylbis[1,1-diphenyl-
SOL 108-88-3 PhMe

STAGE(2)
RCT DY 24424-99-5
SOL 75-09-2 CH2Cl2

PRO GK 444620-33-1

L9 ANSWER 3 OF 21 CASREACT COPYRIGHT 2007 ACS on STN

RX(8) OF 78 T + N ===> U...



YIELD 97%

RX(8) RCT T 24424-99-5, N 110-85-0

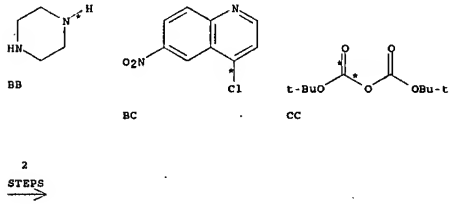
STAGE(1)
SOL 67-63-0 Me2CHOH

STAGE(2)
RGT R 110-15-6 Butanedioic acid

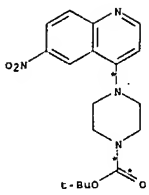
PRO U 57260-71-6

L9 ANSWER 4 OF 21 CASREACT COPYRIGHT 2007 ACS on STN

RX(48) OF 134 COMPOSED OF RX(25), RX(35)
RX(48) BB + BC + CC ===> CD



2
STEPS



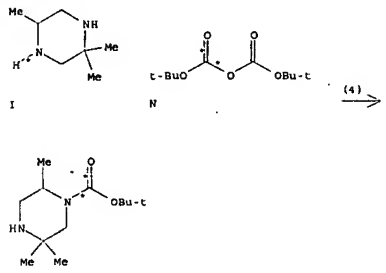
CD
YIELD 96%

RX(25) RCT BB 110-85-0, BC 13675-94-0
PRO BD 227957-03-1
SOL 108-88-3 PhMe

RX(35) RCT BD 227957-03-1, CC 24424-99-5
RGT CE 584-08-7 K2CO3
PRO CD 227957-04-2
SOL 7732-18-5 Water, 109-99-9 THF

L9 ANSWER 5 OF 21 CASREACT COPYRIGHT 2007 ACS on STN

RX(4) OF 401 ...I + N ===> O...



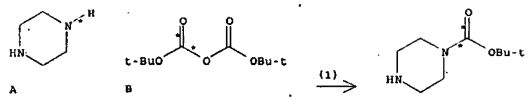
I N

O
YIELD 57%

RX(4) RCT I 139139-56-3, N 24424-99-5
PRO O 308109-96-8
SOL 109-99-9 THF
NTE chemoselective

L9 ANSWER 6 OF 21 CASREACT COPYRIGHT 2007 ACS on STN

RX(1) OF 36 A + B ===> C

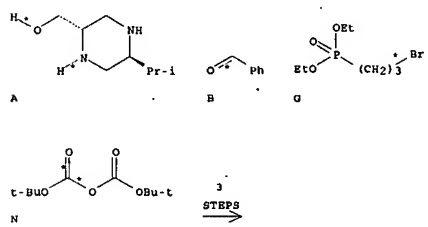


A B C
YIELD 83%

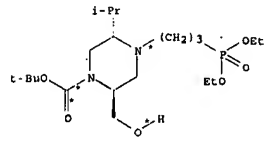
RX(1) RCT A 110-85-0, B 24424-99-5
PRO C 57260-71-6
SOL 75-09-2 CH2Cl2

L9 ANSWER 7 OF 21 CASREACT COPYRIGHT 2007 ACS on STN

RX(23) OF 42 COMPOSED OF RX(1), RX(3), RX(5)
RX(23) A + B + G + N ===> O



A B G N



O
YIELD 97%

RX(1) RCT A 155322-94-4, B 100-52-7
PRO C 192210-50-7
SOL 71-43-2 Benzene
NTE mol. sieves agent

RX(3) RCT C 192210-50-7, G 1186-10-3

STAGE(1)
RGT I 497-19-8 Na2CO3
SOL 67-56-1 MeOH

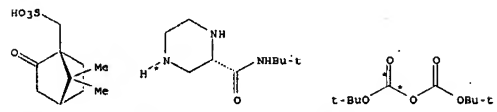
STAGE(2)
RGT J 7647-01-0 HCl
SOL 7732-18-5 Water

PRO H 192210-52-9

RX(5) RCT H 192210-52-9, N 24424-99-5
RGT I 497-19-8 Na2CO3
PRO O 192210-54-1
CAT 5470-11-1 H2NOH-HCl
SOL 75-09-2 CH2Cl2, 7732-18-5 Water

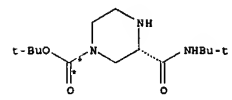
L9 ANSWER 8 OF 21 CASREACT COPYRIGHT 2007 ACS on STN

RX(8) OF 89 ...AC + AD ===> V...



AC: CM 1 AC: CM 2 AD

(8)

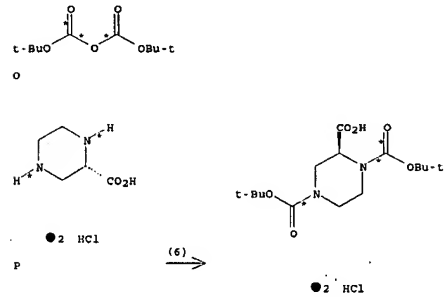


V
YIELD 77%

RX(8) RCT AC 166941-48-6, AD 24424-99-5
RGT O 121-44-8 Et3N
PRO V 150323-35-6
SOL 64-17-5 EtOH, 141-78-6 AcOEt

L9 ANSWER 9 OF 21 CASREACT COPYRIGHT 2007 ACS on STN

RX(6) OF 15 O + P ===> A...

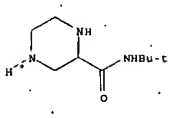


O P A
●2 HCl
YIELD 92%

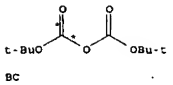
RX(6) RCT O 24424-99-5, P 158663-69-5
RGT Q 121-44-8 Et3N
PRO A 173774-47-5
SOL 67-56-1 MeOH
NTE 50°, overnight

L9 ANSWER 10 OF 21 CASREACT COPYRIGHT 2007 ACS on STN

RX(18) OF 134 ...AZ + BC ===> K...

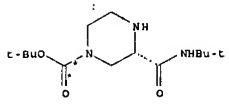


AZ



BC

(18) ⟹



K

RX(18) RCT AZ 121885-09-4

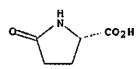
STAGE(1)
RGT BD 3144-16-9 10-CSA
SOL 71-23-8 PrOH, 7732-18-5 Water, 75-05-8 MeCN

STAGE(2)
RCT BC 24424-99-5
RGT AB 121-44-8 Et3N
SOL 64-17-5 EtOH, 141-78-6 AcOEt

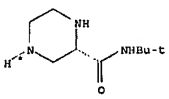
PRO K 150323-35-6

L9 ANSWER 11 OF 21 CASREACT COPYRIGHT 2007 ACS on STN

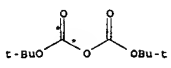
RX(4) OF 135 ...S + T ===> U...



S: CM 1

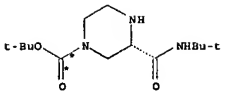


S: CM 2



T

(4) ⟹



U
YIELD 74%

RX(4) RCT S 166941-49-7

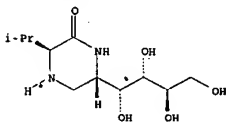
STAGE(1)
RGT E 121-44-8 Et3N
SOL 71-23-8 PrOH

STAGE(2)
RCT T 24424-99-5
SOL 141-78-6 AcOEt

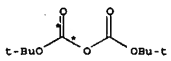
PRO U 150323-35-6

L9 ANSWER 12 OF 21 CASREACT COPYRIGHT 2007 ACS on STN

RX(5) OF 38 ...J + P ===> A...

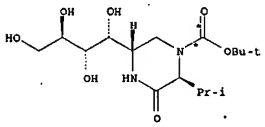


J



P

(5) ⟹

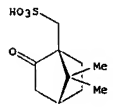


A
YIELD 87%

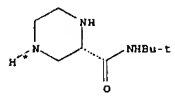
RX(5) RCT J 168140-07-6, P 24424-99-5
PRO A 168140-01-0
SOL 67-56-1 MeOH

L9 ANSWER 13 OF 21 CASREACT COPYRIGHT 2007 ACS on STN

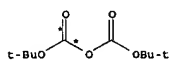
RX(3) OF 176 ...L + M ===> N...



L: CM 1

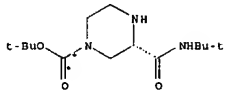


L: CM 2



M

(3) ⟹

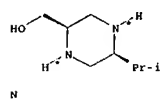


N
YIELD 77%

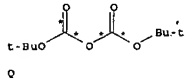
RX(3) RCT L 166941-48-6, M 24424-99-5
RGT E 121-44-8 Et3N
PRO N 150323-35-6
SOL 64-17-5 EtOH, 141-78-6 AcOEt
NTE alternative preparation shown

L9 ANSWER 14 OF 21 CASREACT COPYRIGHT 2007 ACS on STN

RX(5) OF 25 ...N + Q ===> R...

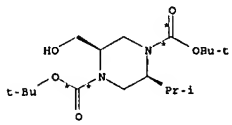


N



Q

(5) ⟹

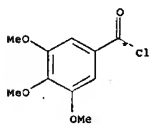


R
YIELD 87%

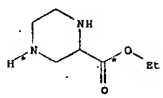
RX(5) RCT N 155225-20-0, Q 24424-99-5
PRO R 159010-58-9
SOL 75-05-8 MeCN

L9 ANSWER 15 OF 21 CASREACT COPYRIGHT 2007 ACS on STN

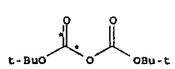
RX(44) OF 130 COMPOSED OF RX(2), RX(5)
RX(44) I + J + T ===> U



I

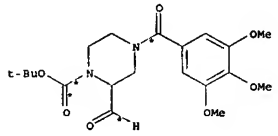


J



T

2
STEPS ⟹



U
YIELD 82%

RX(2) RCT I 4521-61-3, J 89941-07-1
RGT L 121-44-8 Et3N
PRO K 129798-93-2
SOL 75-09-2 CH2Cl2

RX(5) RCT T 24424-99-5, K 129798-93-2

STAGE(1)
RGT L 121-44-8 Et3N
SOL 75-09-2 CH2Cl2

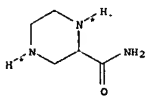
STAGE(2)
RGT E 16940-66-2 NaBH4, V 7447-41-8 LiCl
SOL 64-17-5 EtOH, 109-99-9 THF

STAGE(3)
RGT W 67-68-5 DMSO, L 121-44-8 Et3N, X 79-37-8 (COCl)2
SOL 75-09-2 CH2Cl2

PRO U 129799-20-8
NTE Swern oxidn. in third stage

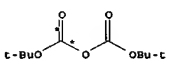
L9 ANSWER 16 OF 21 CASREACT COPYRIGHT 2007 ACS on STN

RX(4) OF 12 ...P + Q + R ===> S...



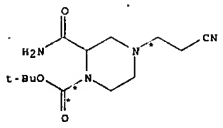
P

Q



R

(4)



S
YIELD 35%

RX(4) RCT P 84501-64-4, Q 2417-90-5

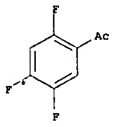
STAGE(1)
RGT T 7087-68-5 EtN(Pr-i)2
SOL 64-17-5 EtOH

STAGE(2)
RCT R 24424-99-5

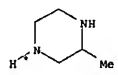
PRO S 128504-84-7

L9 ANSWER 17 OF 21 CASREACT COPYRIGHT 2007 ACS on STN

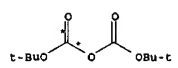
RX(6) OF 15 COMPOSED OF RX(2), RX(3)
RX(6) E + F + J ===> K



E

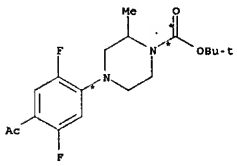


F



J

2 STEPS



K
YIELD 87%

RX(2) RCT E 129322-83-4, F 109-07-9

STAGE(1)
SOL 110-86-1 Pyridine, 121-44-8 Et3N

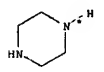
STAGE(2)
RGT C 7647-01-0 HCl

PRO G 144647-65-4

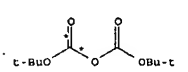
RX(3) RCT G 144647-65-4, J 24424-99-5
RGT I 121-44-8 Et3N
PRO K 144647-66-5
SOL 75-09-2 CH2Cl2

L9 ANSWER 18 OF 21 CASREACT COPYRIGHT 2007 ACS on STN

RX(43) OF 110 BV + BS ===> P...

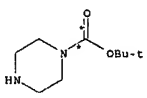


BV



BS

(43)

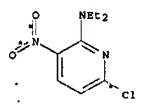


P
YIELD 79%

RX(43) RCT BV 110-85-0, BS 24424-99-5
PRO P 57260-71-6
SOL 75-65-0 t-BuOH

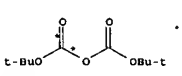
L9 ANSWER 19 OF 21 CASREACT COPYRIGHT 2007 ACS on STN

RX(19) OF 27 COMPOSED OF RX(4), RX(5), RX(11)
RX(19) J + E + AM ===> S



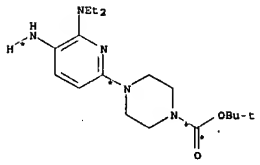
J

E



AM

3 STEPS



S
YIELD 95%

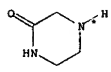
RX(4) RCT J 125173-52-6, E 110-85-0
RGT K 584-08-7 K2CO3
PRO M 125173-54-8
SOL 75-05-8 MeCN

RX(5) RCT M 125173-54-8
RGT O 1333-74-0 H2, P 7647-01-0 HCl
PRO N 125173-55-9
CAT 7440-05-3 Pd
SOL 64-17-5 EtOH

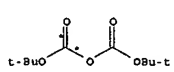
RX(11) RCT N 125173-55-9, AM 24424-99-5
RGT AC 121-44-8 Et3N
PRO S 125173-56-0
SOL 75-09-2 CH2Cl2

L9 ANSWER 20 OF 21 CASREACT COPYRIGHT 2007 ACS on STN

RX(6) OF 29 L + M ===> A...

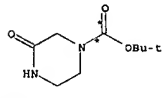


L



M

(6)

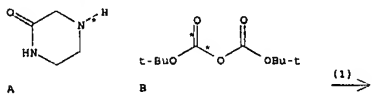


A

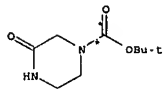
RX(6) RCT L 5625-67-2, M 24424-99-5
PRO A 76003-29-7

L9 ANSWER 21 OF 21 CASREACT COPYRIGHT 2007 ACS on STN

RX(1) OF 14 A + B ===> C....



A B



C

RX(1) RCT A 5625-67-2, B 24424-99-5
PRO C 76003-29-7

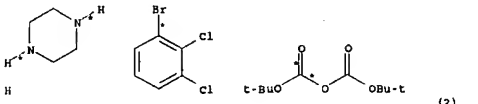
=> d ibib abs fhit

L9 ANSWER 1 OF 21 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 138:271642 CASREACT
TITLE: Progress in arylpiperazine synthesis by the catalytic amination reaction
AUTHOR(S): Torisawa, Yasuhiro; Nishi, Takao; Minamikawa, Jun-ichi
CORPORATE SOURCE: Process Research Laboratory, Second Tokushima Factory, Otsuka Pharmaceutical Co. Ltd., Kawauchi-cho, Tokushima, 771-0182, Japan
SOURCE: Bioorganic & Medicinal Chemistry (2002), 10(12), 4023-4027
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

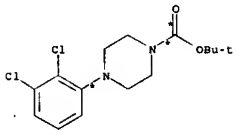
AB Careful base and solvent optimization for catalytic amination is described. A Pd-catalyzed amination between some aryl bromide and unprotected piperazine (1 equiv) was efficiently carried out with Pd/BINAP catalyst in a toluene-DBU solvent system, which is useful for the one-pot preparation of unsym. piperazine through amination and in-situ N-protection. Reaction with N-BOC-piperazine was also successful in toluene-DBU or more polar NMP with Cs2CO3 as a key base. No reports have previously reported

such solvent and base optimization in arylpiperazine synthesis.

RX(2) OF 3 H + A + I ===> C



H A I



C
YIELD 75%

RX(2) RCT H 110-85-0, A 56961-77-4

STAGE(1)
SOL 108-88-3 PhMe
CON 10 minutes, 40 deg C

STAGE(2)
CAT 98327-87-8 Phosphine, 1,1'-[1,1'-binaphthalene]-2,2'-diylbis[1,1-diphenyl-, 51364-51-3 Ph2-pentadienone Pd

STAGE(3)
RGT J 6674-22-2 DBU
CON 5 minutes, 60 - 70 deg C

STAGE(4)
RGT K 865-48-5 NaOBu-t
CON 1 - 4 hour

STAGE(5)
RCT I 24424-99-5

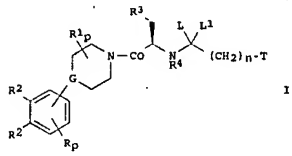
PRO C 503315-03-5
NTE yield depends on cat. and base
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs fhit 2-21

L9 ANSWER 2 OF 21 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 137:140776 CASREACT
TITLE: Preparation of piperidinyl and piperazinyl amino acid derivatives as melanocortin receptor agonists
INVENTOR(S): Backer, Ryan Thomas; Briner, Karin; Doecke, Christopher William; Fisher, Matthew Joseph; Kuklish, Steven Lee; Mancuso, Vincent; Martinelli, Michael John; Mullaney, Jeffrey Thomas; Xie, Chaoyu
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 263 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002059107	A1	20020801	WO 2002-US516	20020123
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2433025	A1	20020801	CA 2002-2433025	20020123
AU 2002235323	A1	20020806	AU 2002-235323	20020123
EP 1368339	A1	20031210	EP 2002-701923	20020123
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004521117	T	20040715	JP 2002-559409	20020123
US 2004058936	A1	20040325	US 2003-466249	20030711
US 7157463	B2	20070102		
IN 2003KN00913	A	20050311	IN 2003-KN913	20030716
PRIORITY APPLN. INFO.:			US 2001-263595P	20010123
			WO 2002-US516	20020123

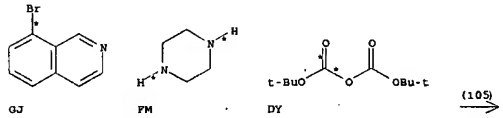
OTHER SOURCE(S): MARPAT 137:140776
GI



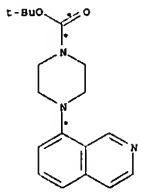
I

AB The invention relates to melanocortin receptor (MC-R) agonists I [G = CR1 or N; LL1 = H2 or oxo; T = isoquinolinyl or tetrahydro derivative, isoindolinyl, or piperazinyl; n = 0-8; R = H, OH, CN, NO2, halo, alkyl, acyl, etc.; R1 = H, alkyl, alkylcarbamoyl, (D)phenyl, (D)cycloalkyl, or oxo (unless amide is formed); p = 0-4; CR2CR2 is a 5- or 6-membered carbocycle optionally substituted by 1-3 groups R; R3 = (un)substituted aryl or thienyl; R4 = H, alkyl, acyl, cycloalkyl, or alkoxyalkyl], or their pharmaceutically-acceptable salts or stereoisomers, which are useful in the treatment of obesity, diabetes, and male and/or female sexual dysfunction. Compds. I comprise three domains, i.e., a piperidino or piperazinyl fragment, an amino acid, and a radical CLL1(CH2)n-T. Thus, 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid [1-(4-chlorobenzyl)-2-[4-[2-(methylsulfonyl)-1,2,3,4-tetrahydroisoquinolin-8-yl]piperazin-1-yl]-2-oxoethyl]amide (claimed compound) was prepared via acylation of the piperazine moiety.

RX(105) OF 794 GJ + FM + DY ===> GK...



GJ FM DY



GK
YIELD 83%

RX(105) KCT GJ 63927-22-0, FM 110-85-0

STAGE(1)
RGT BF 865-48-5 NaOBu-t
CAT 51364-51-3 Ph2-pentadienone Pd, 98327-87-8 Phosphine, 1,1'-[1,1'-binaphthalene]-2,2'-diylbis[1,1-diphenyl-
SOL 108-88-3 PhMe

STAGE(2)
RCT DY 24424-99-5
SOL 75-09-2 CH2Cl2

PRO GK 444620-33-1
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 21 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 136:183836 CASREACT
TITLE: Preparation of homodimeric, heterodimeric and/or homo- and heteromultimeric prodrugs for treatment of phosphodiesterase-mediated diseases or dysfunction.
INVENTOR(S): Russo, Elisa Mannochio de Souza; Russo, Valter Freire Torres
PATENT ASSIGNEE(S): Cristalia Productos Quimicos e Farmaceuticos Ltda., Brazil; Pacheco, Ogari De Castro
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002012241	A1	20020214	WO 2001-BR96	20010807
WO 2002012241	A8	20031204		

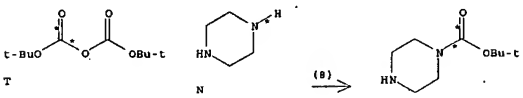
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,

ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

BR 2000003386	A	20040706	BR 2000-3386	20000808
AU 200176200	A	20020218	AU 2001-76200	20010807
EP 1315729	A1	20030604	EP 2001-953709	20010807
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004106629	A1	20040603	US 2003-362602	20030321
US 7148350	B2	20061212		
PRIORITY APPLN. INFO.:			BR 2000-3386	20000808
			WO 2001-BR96	20010807

OTHER SOURCE(S): MARPAT 136:183836
AB Homodimeric, heterodimeric, and/or homo- and heteromultimeric pro-drugs in which the monomeric units are bonded to each other or to a polymeric matrix or container by means of labile bridges, are claimed. The monomeric units are derivs. of 1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidine-7-one. Thus, 4-nitrophenyl chloroformate in CH2Cl2 at 0° was treated with 5-[2-ethoxy-5-[(4-hydroxyethyl-1-piperazinyl)sulfonyl]phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one in CH2Cl2 and then with Et3N and dimethylaminopyridine followed by reflux to give 85% carbonate homodimer product.

RX(8) OF 78 T + N ===> U...



T N U
YIELD 97%

RX(8) RCT T 24424-99-5, N 110-85-0

STAGE(1)
SOL 67-63-0 Me2CHOH

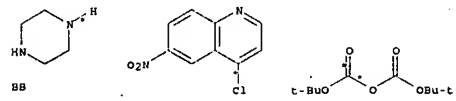
STAGE(2)
RGT R 110-15-6 Butanedioic acid

PRO U 57260-71-6
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 21 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 136:112207 CASREACT

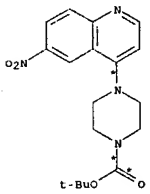
TITLE: Novel (4-piperazin-1-ylquinolin-6-yl) arylsulfonamides with high affinity and selectivity for the 5-HT6 receptor
AUTHOR(S): Bromidge, S. M.; Griffith, K.; Heightman, T. D.; Jennings, A.; King, F. D.; Moss, S. F.; Newman, H.; Riley, G.; Routledge, C.; Serafinowska, H. T.; Thomas, D. R.
CORPORATE SOURCE: Discovery Research Europe, GlaxoSmithKline, Discovery Chemistry, Harlow, Essex, CM19 5AW, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(21), 2843-2846
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The discovery of (4-piperazin-1-ylquinolin-6-yl) arylsulfonamides and their binding affinities for a selection of 5-HT and dopamine subreceptors is described. Many compds. show high affinity (pKi>8) for the 5-HT6 receptor and >100-fold selectivity against a range of other receptors. Structure-activity relationships of these compds. are discussed.

RX(48) OF 134 COMPOSED OF RX(25), RX(35)
RX(48) BB + BC + CC ===> CD



BB BC CC

2
STEPS



CD
YIELD 96%

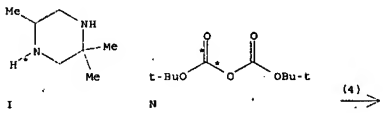
RX(25) RCT BB 110-85-0, BC 13675-94-0
PRO BD 227957-03-1
SOL 108-88-3 PhMe

RX(35) RCT BD 227957-03-1, CC 24424-99-5
RGT CE 584-08-7 K2CO3
PRO CD 227957-04-2
SOL 7732-18-5 Water, 109-99-9 THF
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

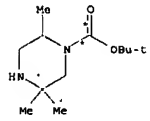
L9 ANSWER 5 OF 21 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 134:4912 CASREACT
TITLE: New Diarylmethylpiperazines as Potent and Selective Nonpeptidic δ Opioid Receptor Agonists with Increased In Vitro Metabolic Stability
AUTHOR(S): Plobeck, Niklas; Delorme, Daniel; Wei, Zhong-Yong; Yang, Hua; Zhou, Fei; Schwarz, Peter; Gawell, Lars; Gagnon, Helene; Pelcman, Benjamin; Schmidt, Ralf; Yue, Shi Yi; Walpole, Christopher; Brown, William; Zhou, Edward; Labarre, Maryse; Payza, Kemal; St-Onge, Stephane; Kamassah, Augustus; Morin, Pierre-Emmanuel; Projean, Denis; Ducharme, Julie; Roberts, Edward
CORPORATE SOURCE: Departments of Chemistry and Pharmacology, Astra Zeneca R&D Montreal, Saint-Laurent, QC, H4S 1Z9, Can.
SOURCE: Journal of Medicinal Chemistry (2000), 43(21), 3878-3894
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Nonpeptide δ opioid agonists are analgesics with a potentially improved side-effect and abuse liability profile, compared to classical opioids. Andrews anal. of the NIH nonpeptide lead SNC-80 suggested the removal of substituents not predicted to contribute to binding. This approach led to a simplified lead, N,N-diethyl-4-[phenyl(1-piperazinyl)methyl]benzamide which retained potent binding affinity and selectivity to the human δ receptor (IC50 = 11 nM, μ/δ =

740, <δ > 900) and potency as a full agonist (EC50 = 36 nM) but had a markedly reduced mol. weight, only one chiral center, and increased in vitro metabolic stability. From this lead, the key pharmacophore groups for δ receptor affinity and activation were more clearly defined by SAR and mutagenesis studies. Further structural modifications confirmed the importance of the N,N-diethylbenzamide group and the piperazine lower basic nitrogen for δ binding, in agreement with mutagenesis data. A number of piperazine N-alkyl substituents were tolerated. In contrast, modifications of the Ph group led to the discovery of a series of diarylmethylpiperazines exemplified by N,N-diethyl-4-[1-piperazinyl(8-quinolinyl)methyl]benzamide which had an improved in vitro binding profile (IC50 = 0.5 nM, μ/δ = 1239, EC50 = 3.6 nM) and increased in vitro metabolic stability compared to SNC-80.

RX(4) OF 401 ...I + N ===> O...



I N (4) ⟹



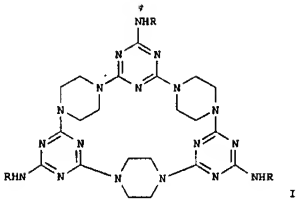
O

YIELD 57%

RX(4) RCT I 139139-56-3, N 24424-99-5
PRO O 308109-96-8
SOL 109-99-9 THF
NTE chemoselective
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 21 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 133:4637 CASREACT
TITLE: A stepwise synthesis of triazine-based macrocyclic scaffolds
AUTHOR(S): Lowik, Dennis W. P. M.; Lowe, Christopher R.
CORPORATE SOURCE: Institute of Biotechnology, University of Cambridge, Cambridge, CB2 1QT, UK

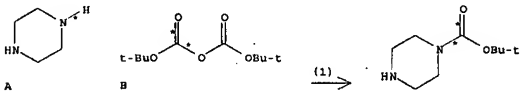
SOURCE: Tetrahedron Letters (2000), 41(11), 1837-1840
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The synthesis of the non-peptidic triazine-based macrocyclic scaffold I [R, R1, R2 = amyl; R = amyl, R1 = CH2CHMe2, R2 = CH2Ph; R = (CH2)2Ph, R1 = amyl, R2 = CH2Ph, Ph, (CH2)2Ph; R, R1, R2 = (CH2)2Ph; R, R1 = (CH2)2Ph, R2 = amyl; R, R1, R2 = dodecyl] is presented. The strategy employed allows for the facile functionalization of the macrocyclic mols. and combinatorial construction of putative receptor mols.

RX(1) OF 36 A + B ===> C

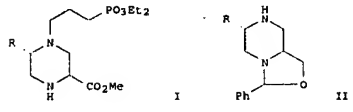


A B (1) ⟹ C

YIELD 83%

RX(1) RCT A 110-85-0, B 24424-99-5
PRO C 57260-71-6
SOL 75-09-2 CH2Cl2
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

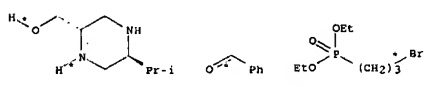
L9 ANSWER 7 OF 21 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 127:95555 CASREACT
TITLE: General approach to the synthesis of optically active 2-carboxy-4-[3'-(diethoxyphosphinyl)propyl]-5-alkylpiperazines (CPP analogs)
AUTHOR(S): Falorni, Massimo; Porcheddu, Andrea; Giacomelli, Giampaolo
CORPORATE SOURCE: Dipartimento di Chimica, Universita di Sassari, Sassari, I-07100, Italy
SOURCE: Tetrahedron: Asymmetry (1997), 8(10), 1633-1639
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



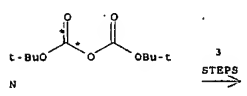
I II

AB General stereospecific syntheses of optically active carboxy-4-[3'-(diethoxyphosphinyl)propyl]-5-alkylpiperazines (CPP analogs) I [R = iso-Pr (2S,5S), iso-Bu (2R,5S)] are described. The methods are based on the protection and alkylation of 5-alkyl-2-hydroxymethylpiperazines as their N,O-acetonide derivs. II (R= iso-Pr, iso-Bu). The procedures presented are based on readily available starting materials, such as piperazine alcs., and can be arranged for multigram quantities.

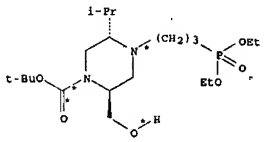
RX(23) OF 42 COMPOSED OF RX(1), RX(3), RX(5)
RX(23) A + B + G + N ===> O



A B G



N 3 STEPS ⟹



O

YIELD 97%

RX(1) RCT A 155322-94-4, B 100-52-7
PRO C 192210-50-7
SOL 71-43-2 Benzene
NTE mol. sieves agent

RX(3) RCT C 192210-50-7, G 1186-10-3

STAGE(1)
RGT I 497-19-8 Na2CO3
SOL 67-56-1 MeOH

STAGE(2)
RGT J 7647-01-0 HCl
SOL 7732-18-5 Water

PRO H 192210-52-9

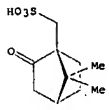
RX(5) RCT H 192210-52-9, N 24424-99-5
RGT I 497-19-8 Na2CO3
PRO O 192210-54-1
CAT 5470-11-1 H2NOH-HCl
SOL 75-09-2 CH2Cl2, 7732-18-5 Water
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 21 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 126:58943 CASREACT
TITLE: Quantitative conversion of indene to (1S,2R) indene oxide and (1S,2R)-indanediol by combination of haloperoxidase bioconversion and chemical steps
INVENTOR(S): Chartrain, Michel M.; Connors, Neal C.; Garrity, George M.; Olewinski, Roger C., Jr.; Verhoeven, Thomas R.; Zhang, Jinyou
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

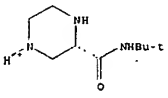
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9636724	A1	19961121	WO 1996-US6954	19960515
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5605819	A	19970225	US 1995-445154	19950519
AU 9657497	A	19961129	AU 1996-57497	19960515
CN 1190994	A	19980819	CN 1996-195618	19960515
CN 1066772	B	20010606		
BR 9608720	A	19990629	BR 1996-8720	19960515
PRIORITY APPLN. INFO.:			US 1995-445154	19950519
			WO 1996-US6954	19960515

AB A process is disclosed that quant. bioconverts indene to (1S,2R)-indene oxide and (1S,2R)-indanediol by the action of fungal haloperoxidase followed by various chemical step(s), e.g., adjusting the pH.

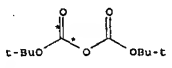
RX(8) OF 89 ...AC + AD ===> V...



AC: CM 1

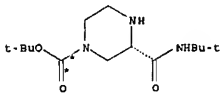


AC: CM 2



AD

(8)



V
YIELD 77%

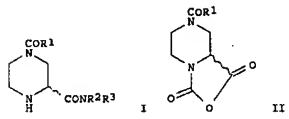
RX(8) RCT AC 166941-48-6, AD 24424-99-5
RGT O 121-44-8 Et3N
PRO V 150323-35-6
SOL 64-17-5 EtOH, 141-78-6 AcOEt

L9 ANSWER 9 OF 21 CASREACT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 124:176151 CASREACT
TITLE: Preparation of 3-carbamoylpiperazine-1-carboxylic acid derivatives.
INVENTOR(S): Brieden, Walter; Roduit, Jean-Paul
PATENT ASSIGNEE(S): Lonza AG, Switz.
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9529169	A2	19951102	WO 1995-EP1475	19950419
WO 9529169	A3	19951221		
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2186023	A1	19951102	CA 1995-2186023	19950419
CA 2186023	C	20061107		
EP 756593	A1	19970205	EP 1995-918571	19950419
EP 756593	B1	20000920		
R: AT, BE, CH, DE, DK, ES, FR, GB, IE, IT, LI, NL, PT, SE				
JP 09512028	T	19971202	JP 1995-527340	19950419
AT 196469	T	20001015	AT 1995-918571	19950419
ES 2151960	T3	20010116	ES 1995-918571	19950419
PT 756593	T	20010131	PT 1995-918571	19950419
US 5856485	A	19990105	US 1996-722149	19961223
PRIORITY APPLN. INFO.:			CH 1994-1205	19940420
			WO 1995-EP1475	19950419

OTHER SOURCE(S): MARPAT 124:176151
GI

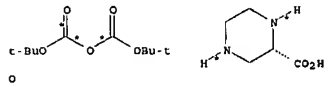


I II

AB Title compds. [I; R1 = (substituted) alkyl, OR4, amino; R2, R3 = H, (substituted) alkyl, alkenyl, aryl, amino acid (ester) residue; R4 = (substituted) alkyl, alkenyl, aryl] in the form of enantiomers or enantiomer mixts. were prepared by N-acylation of a piperazine-2-carboxylic acid or a salt thereof followed by treatment with a halogenating agent to form a piperazine carboxylic acid anhydride (II), which was then treated with HNR2R3. Thus, (S)-2-piperazinecarboxylic acid dihydrochloride in MeOH was treated with Et3N and di-tert-butyldicarbonate followed by stirring overnight at 50° to give 92% (S)-piperazine-1,2,4-tricarboxylic acid 1,4-di-tert-Bu ester. The latter in THF was treated with pyridine, DMF, and SOCl2 followed by stirring for 4 h at 40° to give 81% (S)-1,3-dioxotetrahydrooxazo[3,4-a]piperazin-7-carboxylic acid

tert-Bu ester. This was refluxed with tert-butylamine in CH2Cl2 to give 82% (S)-3-(tert-butylcarbamoyl)piperazin-1-carboxylic acid tert-Bu ester.

RX(6) OF 15 O + P ===> A...

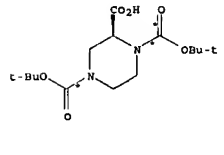


O

●2 HCl

P

(6)



●2 HCl

A
YIELD 92%

RX(6) RCT O 24424-99-5, P 158663-69-5
RGT Q 121-44-8 Et3N
PRO A 173774-47-5
SOL 67-56-1 MeOH
NTE 50°, overnight

L9 ANSWER 10 OF 21 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 123:314022 CASREACT
TITLE: Piperazinylpentanamide derivatives useful as HIV protease inhibitors
INVENTOR(S): Huff, Joel R.; Vacca, Joseph P.; Dorsey, Bruce D.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9516688	A1	19950622	WO 1994-US14187	19941212
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, UZ				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2178760	A1	19950622	CA 1994-2178760	19941212
CA 2178760	C	20000801		
AU 9514331	A	19950703	AU 1995-14331	19941212
AU 692509	B2	19980611		
EP 734387	A1	19961002	EP 1995-905886	19941212
EP 734387	B1	20020410		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
HU 74681	A2	19970128	HU 1996-1649	19941212
CN 1142827	A	19970212	CN 1994-194954	19941212
CN 1046727	B	19991124		
BR 9408305	A	19970826	BR 1994-8305	19941212
RU 2137768	C1	19990920	RU 1996-114986	19941212
JP 3000564	B2	20000117	JP 1995-516855	19941212
JP 09506619	T	19970630		
CZ 288312	B6	20010516	CZ 1996-1586	19941212
AT 215952	T	20020415	AT 1995-905886	19941212
ES 2174921	T3	20021116	ES 1995-905886	19941212
US 5646148	A	19970708	US 1995-412509	19950329
FI 9602488	A	19960614	FI 1996-2488	19960614
US 5807841	A	19980915	US 1997-825787	19970408
PRIORITY APPLN. INFO.:			US 1993-168013	19931215
			US 1993-170475	19931220
			WO 1994-US14187	19941212
			US 1995-412509	19950329

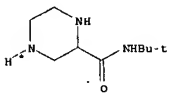
OTHER SOURCE(S): MARPAT 123:314022
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

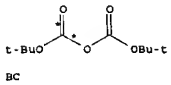
AB Compds. of formula I [X = stable (un)saturated 8- to 10-membered bicyclic heterocycle, containing 1-3 of N, S, or O, and (un)substituted by OH, halo, alkyl, or oxo; with 3 exceptions], useful as HIV protease inhibitors, are claimed, and an example preparation is given. I are useful in the prevention or treatment of infection by HIV and in the treatment of AIDS, alone or in combination with other antivirals, immunomodulators, antibiotics or vaccines. For example, furanone II underwent lithiation and stereoselective benzylation, followed by desilylation, conversion of the resulting alc. to a triflate, and coupling with a corresponding piperazine derivative [large-scale preparation given] to yield intermediate III. Hydrolysis of the lactone function, silylation of the formed alc., amidation of the carboxy function with the corresponding aminohydroxyindane, desilylation, removal of the BOC group, and finally alkylation with 3-(chloromethyl)furo[2,3-b]pyridine HCl, gave title compound I [X = Q]. The latter inhibited HIV protease in vitro with IC50 of approx. 0.27 nM, and

inhibited HIV spread in a cell culture with CIC95 of 25 nM.

RX(18) OF 134 ...AZ + BC ===> K...

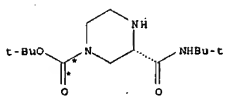


AZ



BC

(18) ⟹



K

RX(18) RCT AZ 121885-09-4

STAGE(1)
RGT BD 3144-16-9 10-CSA
SOL 71-23-8 PrOH, 7732-18-5 Water, 75-05-8 MeCN

STAGE(2)
RCT BC 24424-99-5
RGT AB 121-44-8 Et3N
SOL 64-17-5 EtOH, 141-78-6 AcOEt

PRO K 150323-35-6

L9 ANSWER 11 OF 21 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 123:228214 CASREACT
TITLE: Process for making HIV protease inhibitors
INVENTOR(S): Askin, David; Reider, Paul; Rossen, Kai; Varsolona, Richard J.; Wells, Kenneth M.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9502583	A1	19950126	WO 1994-US7695	19940711

W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, GE, HU, JP, KE, KG, KR, KZ, LK, LT, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, UZ
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

IL 110255	A	19981206	IL 1994-110255 19940708
CA 2167408	A1	19950126	CA 1994-2167408 19940711
CA 2167408	C	20030916	
AU 9473267	A	19950213	AU 1994-73267 19940711
AU 679770	B2	19970710	
EP 708763	A1	19960501	EP 1994-923392 19940711
EP 708763	B1	20030226	

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE

CN 1130905	A	19960911	CN 1994-193331 19940711
CN 1046715	B	19991124	
JP 09500131	T	19970107	JP 1994-504630 19940711
HU 76789	A2	19971128	HU 1996-78 19940711
RU 2134263	C1	19990810	RU 1996-105392 19940711
RO 117019	B1	20010928	RO 1996-68 19940711
RO 117175	B1	20011130	RO 2001-2001004121 19940711
RO 117176	B1	20011130	RO 2001-2001004141 19940711
AT 233249	T	20030315	AT 1994-923392 19940711
EP 1310495	A2	20030514	EP 2003-75406 19940711
EP 1310495	A3	20030521	

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI

ES 2191683	T3	20030916	ES 1994-923392 19940711
ZA 9405194	A	19950215	ZA 1994-5194 19940715
US 5618939	A	19970408	US 1995-474926 19950607
US 5637711	A	19970610	US 1995-474626 19950607
US 5693803	A	19971202	US 1995-474800 19950607
FI 9600206	A	19960314	FI 1996-206 19960116
US 5861512	A	19990119	US 1997-929970 19970916

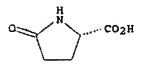
PRIORITY APPLN. INFO.: US 1993-92627 19930716
EP 1994-923392 19940711
WO 1994-US7695 19940711
US 1994-341334 19941216
US 1995-482999 19950607

OTHER SOURCE(S): MARPAT 123:228214
GI

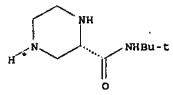
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB HIV protease inhibitor intermediates [I; R1, R2 = H, (un)substituted alkyl, (un)substituted aryl; R3 = H, alkyl, (un)substituted cycloalkyl, (un)substituted aryl, (un)substituted heterocyclyl; R4 = (un)branched (un)substituted alkyl; r = 0-5] are prepared by reacting an epoxide (II) with an amide (III) in the presence of a strong base (e.g., BuLi) at a low temperature (e.g., -76°). The process and I intermediates are useful for synthesizing HIV protease inhibitor compds. (e.g., L-735,524; IV).

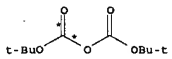
RX(4) OF 135 ...S + T ===> U...



S: CM 1

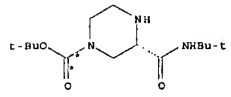


S: CM 2



T

(4) ⟹



U
YIELD 74%

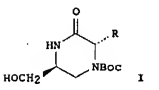
RX(4) RCT S 166941-49-7

STAGE(1)
RGT E 121-44-8 Et3N
SOL 71-23-8 PrOH

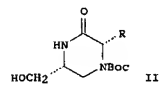
STAGE(2)
RCT T 24424-99-5
SOL 141-78-6 AcOEt

PRO U 150323-35-6

L9 ANSWER 12 OF 21 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 123:228116 CASREACT
TITLE: Synthesis of substituted chiral piperazinones as building blocks for peptidomimetics
AUTHOR(S): Kolter, Thomas; Dahl, Christina; Giannis, Athanassios
CORPORATE SOURCE: Institut Organische Chemie Biochemie, Universitaet Bonn, Bonn, D-53121, Germany
SOURCE: Liebigs Annalen (1995), (4), 625-9
CODEN: LANAEM; ISSN: 0947-3440
PUBLISHER: VCH
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



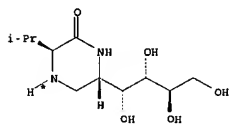
I



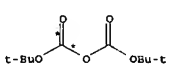
II

AB A new approach to 3,6-disubstituted chiral piperazinones I and II (R = Me2CH, PhCH2, Boc = Me3CO2C) from D-glucosamine hydrochloride or N-Z-D-glucosamine (Z = PhCH2O2C) and L-amino acid derivs. is presented. Both final products and the intermediate pseudopeptides constitute valuable starting materials for the synthesis of peptidomimetics.

RX(5) OF 38 ...J + P ===> A...

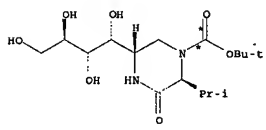


J



P

(5) ⟹



A
YIELD 87%

RX(5) RCT J 168140-07-6, P 24424-99-5
PRO A 168140-01-0
SOL 67-56-1 MeOH

L9 ANSWER 13 OF 21 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 123:143879 CASREACT
TITLE: Process for making HIV protease inhibitors
INVENTOR(S): Askin, David; Volante, Ralph P.; Eng, Kan K.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA

SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9502584	A2	19950126	WO 1994-US7706	19940711
WO 9502584	A3	19950309		
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, FI, GE, HU, JP, KE, KG, KR, KZ, LK, LT, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, UZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5463067	A	19951031	US 1994-187664	19940126
CA 2167183	A1	19950126	CA 1994-2167183	19940711
CA 2167183	C	20051115		
AU 9473588	A	19950213	AU 1994-73588	19940711
AU 676079	B2	19970227		
EP 708762	A1	19960501	EP 1994-922511	19940711
EP 708762	B1	20010328		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 08509985	T	19961022	JP 1994-504632	19940711
RU 2125561	C1	19990127	RU 1996-103642	19940711
PL 179039	B1	20000731	PL 1994-312613	19940711
AT 200079	T	20010415	AT 1994-922511	19940711
SK 282616	B6	20021008	SK 1996-55	19940711
FI 9600184	A	19960314	FI 1996-184	19960115
NO 9600168	A	19960315	NO 1996-168	19960115
GR 3035645	T3	20010629	GR 2001-400119	20010329

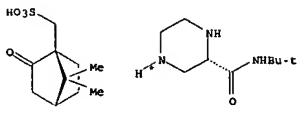
PRIORITY APPLN. INFO.: US 1993-93225 19930716
US 1994-187664 19940126
WO 1994-US7706 19940711

OTHER SOURCE(S): MARPAT 123:143879
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

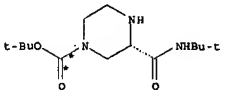
AB Intermediates of formula I [R = H, alkyl, (hydroxy)cycloalkyl, (un)substituted aryl or heterocyclyl; n = 0-5; epoxide has (R) and/or (S) configuration] are prepared by reaction of glycidol or an activated derivative thereof with a corresponding amide. The process, intermediates, and addnl. claimed steps are useful for synthesizing HIV protease inhibitors such as L-735,524 (II). For example, (-)-cis-1-aminoindan-2-ol underwent amidation with PhCH2CH2COCl, followed by cyclization of the resulting amido alc. with 2-methoxypropene, to give 86.4% acetonide III. Reaction of III in THF with either 2(S)-glycidyl tosylate (-56° to -22°) or (S)-epichlorohydrin (-78° to -25°) in the presence of LiN(SiMe3)2 gave (S)-I [R = Ph, n = 1] in 61.2% or 70% yield, resp. This compound was coupled with the protected piperazine derivative IV (Boc = Me3COCO), followed by deprotection of the Boc and oxazolidine functions with aqueous HCl (86.5%), and N-alkylation of the deprotected piperazine with 3-picolyl chloride-HCl and Et3N in DMF (70.7%), to give II as the monohydrate, on a 2-kg scale in the final step.

RX(3) OF 176 ...L + M ===> N...



L; CM 1 L; CM 2 M

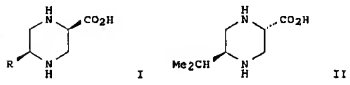
(3)



N
YIELD 77%

RX(3) RCT L 166941-48-6, M 24424-99-5
RGT E 121-44-8 Et3N
PRO N 150323-35-6
SOL 64-17-5 EtOH, 141-78-6 AcOEt
NTE alternative preparation shown

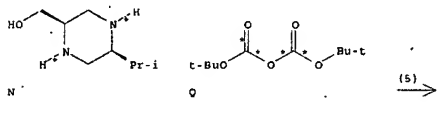
L9 ANSWER 14 OF 21 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 121:301238 CASREACT
TITLE: General and versatile approach to the synthesis of optically active 5-alkylpiperazine-2-carboxylic acids
AUTHOR(S): Falorni, Massimo; Giacomelli, Giampaolo; Satta, Michele; Cossu, Sergio
CORPORATE SOURCE: Dip. Chim., Univ. Sassari, Sassari, I-07100, Italy
SOURCE: Synthesis (1994), (4), 391-5
CODEN: SYNTBF; ISSN: 0039-7881
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I II

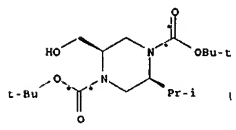
AB General and convenient syntheses of optically active 5-alkylpiperazine-2-carboxylic acids I (R = iso-Pr, isobutyl) are described. The methods are based on cyclization of L- or D-serine with α-amino acids and occur without loss of optical purity. The presented procedures are based on readily available starting materials and can be arranged for multigram quantities.

RX(5) OF 25 ...N + Q ===> R...



N Q

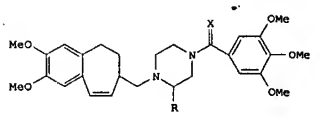
(5)



R
YIELD 87%

RX(5) RCT N 155225-20-0, Q 24424-99-5
PRO R 159010-58-9
SOL 75-05-8 MeCN

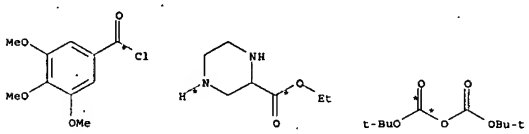
L9 ANSWER 15 OF 21 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 121:108703 CASREACT
TITLE: Synthesis and platelet-activating factor (PAF)-antagonistic activities of trisubstituted piperazine derivatives
AUTHOR(S): Fukushi, Hideto; Mabuchi, Hiroshi; Terashita, Zen-ichi; Nishikawa, Kohei; Sugihara, Hirosada
CORPORATE SOURCE: Pharm. Res. Lab., Takeda Chem. Ind. Ltd., Osaka, 532, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (1994), 42(3), 551-9
CODEN: CPBTAL; ISSN: 0009-2363
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

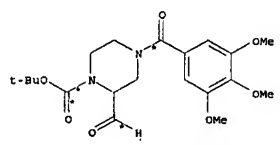
AB 2- Or 3-Substituted 1-(2,3-dimethoxy-6,7-dihydro-5H-benzocyclohepten-8-ylcarbonyl)-4-(3,4,5-trimethoxybenzoyl)- and 4-(3,4,5-trimethoxybenzyl)piperazines (e.g., 2-substituted I) were prepared and evaluated for antagonistic activities against platelet-activating factor (PAF)-induced platelet aggregation and blood pressure reduction The 2-methoxymethyl derivative I (R = 2-CH2OCH3, X = O) (2f) showed the most potent activities in this series. The enantiomers (R)-(+)-2f and (S)-(-)-2f were synthesized from carbobenzoxy-O-benzyl-L- and D-serine in several steps. In the binding expts., (S)-(-)-2f showed thirty times greater affinity than the R isomer for the PAF receptor.

RX(44) OF 130 COMPOSED OF RX(2), RX(5)
RX(44) I + J + T ===> U



I J T

2
STEPS



U
YIELD 82%

aldehyde

RX(2) RCT I 4521-61-3, J 89941-07-1
RGT L 121-44-8 Et3N

PRO K 129798-93-2
SOL 75-09-2 CH2Cl2

RX(5) RCT T 24424-99-5, K 129798-93-2

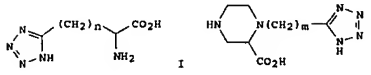
STAGE(1)
RGT L 121-44-8 Et3N
SOL 75-09-2 CH2Cl2

STAGE(2)
RGT E 16940-66-2 NaBH4, V 7447-41-8 LiCl
SOL 64-17-5 EtOH, 109-99-9 THF

STAGE(3)
RGT W 67-68-5 DMSO, L 121-44-8 Et3N, X 79-37-8 (COCl)2
SOL 75-09-2 CH2Cl2

PRO U 129799-20-8
NTE Swern oxidn. in third stage

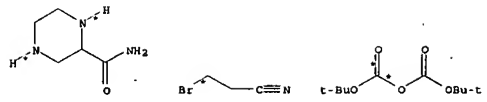
L9 ANSWER 16 OF 21 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 118:213469 CASREACT
TITLE: Tetrazole amino acids as competitive NMDA antagonists
AUTHOR(S): Ornstein, Paul L.; Arnold, M. Brian; Evrard, Debbie; Leander, J. David; Lodge, David; Schoepp, Darryle D.
CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN, 46285, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1993), 3(1), 43-8
CODEN: BMCLE8; ISSN: 0960-894X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



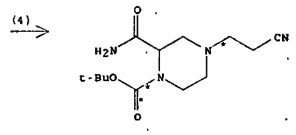
I II

AB The synthesis and pharmacol. characterization of 2 novel series of acidic amino acids, tetrazole-substituted acyclic amino acids I (n = 1-6) and piperazine-2-carboxylic acids II (m = 1-4) as potential N-methyl-D-aspartate (NMDA) receptor antagonists are described. II (m = 2, 3) are potent, systemically active NMDA antagonists.

RX(4) OF 12 ...P + Q + R ===> S...



P Q R



S
YIELD 35%

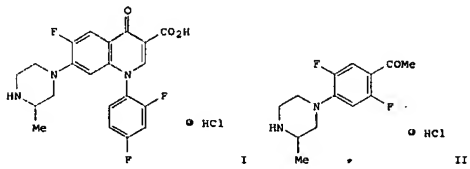
RX(4) RCT P 84501-64-4, Q 2417-90-5

STAGE(1)
RGT T 7087-68-5 EtN(Pr-i)2
SOL 64-17-5 EtOH

STAGE(2)
RCT R 24424-99-5

PRO S 128504-84-7

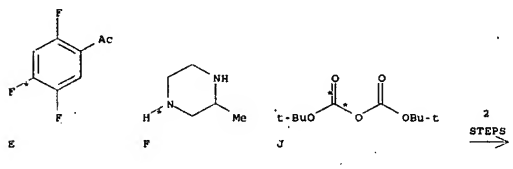
L9 ANSWER 17 OF 21 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 117:251319 CASREACT
TITLE: An alternative synthesis of temafloxacin, a potent antibacterial agent
AUTHOR(S): Chu, Daniel T. W.; Lico, Isabella M.; Claiborne, Akiyo K.; Faubl, Hermann
CORPORATE SOURCE: Anti-Infect. Res. Div., Abbott Lab., Abbott Park, IL, 60064-3500, USA
SOURCE: Canadian Journal of Chemistry (1992), 70(5), 1323-7
CODEN: CJCHAG; ISSN: 0008-4042
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



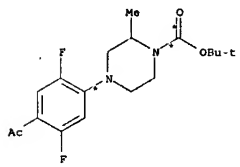
I II

AB An alternative synthesis of (methylpiperazinyl)fluoro(difluorophenyl)dihydrooxoquinolinecarboxylic acid (temafloxacin) hydrochloride I, a potent antibacterial agent, was developed. The method was characterized by regiospecific displacement of the 4-fluoro of the 2,4,5-trifluoroacetophenone by 2-methylpiperazine to produce the key intermediate, 2,5-difluoro-4-(3-methylpiperazin-1-yl)acetophenone (II), which was subsequently converted to I via an intramol. nucleophilic displacement cyclization reaction.

RX(6) OF 15 COMPOSED OF RX(2), RX(3)
RX(6) E + F + J ===> K



E F J



K
YIELD 87%

RX(2) RCT E 129322-83-4, F 109-07-9

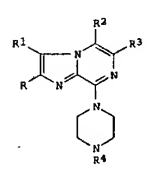
STAGE(1)
SOL 110-86-1 Pyridine, 121-44-8 Et3N

STAGE(2)
RGT C 7647-01-0 HCl

PRO G 144647-65-4

RX(3) RCT G 144647-65-4, J 24424-99-5
RGT I 121-44-8 Et3N
PRO K 144647-66-5
SOL 75-09-2 CH2Cl2

L9 ANSWER 18 OF 21 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 117:191811 CASREACT
TITLE: Synthesis and hypoglycemic activity of substituted 8-(1-piperazinyl)imidazo[1,2-a]pyrazines
AUTHOR(S): Meurer, Laura C.; Tolman, Richard L.; Chapin, Edward W.; Saperstein, Richard; Vicario, Pasquale P.; Zrada, Matthew M.; MacCoss, Malcolm
CORPORATE SOURCE: Merck Sharp and Dohme Res. Lab., Rahway, NJ, 07065, USA
SOURCE: Journal of Medicinal Chemistry (1992), 35(21), 3845-57
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

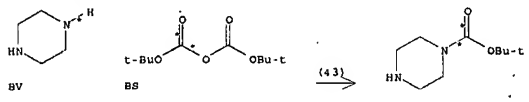


I

AB A series of alkyl- and halo-substituted 8-(1-piperazinyl)imidazo[1,2-a]pyrazines I (R, R2, R4 = H, Me; R1 = H, Cl, Me, Et, Pr, CHMe2, CH2CH2F; R3 = H, Cl, Me), were prepared using two approaches, the condensation of α-halocarbonyl derivs. RC(:X)CHR1Br with an aminopyrazine or the oxidation-dehydration of a [(β-hydroxyalkyl)amino]pyrazine. These imidazo[1,2-a]pyrazines were evaluated for their binding affinity to the α1, α2, β1, and β2 adrenergic receptors as well as their ability to lower blood glucose in insulin resistant hyperglycemic

ob/ob mice. Modifications on 8-(1-piperazinyl)imidazo[1,2-a]pyrazine I (R-R4 = H)(II) reduced α2 binding, lowered hypoglycemic potency, and showed variations in binding to the α1, β1, and β2 adrenergic receptors. In addition to II, the 2-Me, 3-Me, and 5-Me 8-(1-piperazinyl)imidazo[1,2-a]pyrazines, resp.) displayed high affinity for the α2 receptor and were potent hypoglycemic agents when compared to 2-amino-7,8-dihydro-4-(1-piperazinyl)-6H-thiopyrano[3,2-d]pyramidine (MTP-1403). Receptor binding was modified by use of a 4-methylpiperazine moiety which reduced α1 and β1 binding while retaining some hypoglycemic activity. The structure-activity relationship for heterocyclic alkyl and halo substitution on biol. activity is discussed.

RX(43) OF 110 BV + BS ===> P...

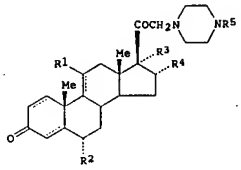


BV BS P

YIELD 79%

RX(43) RCT BV 110-85-0, BS 24424-99-5
PRO P 57260-71-6
SOL 75-65-0 t-BuOH

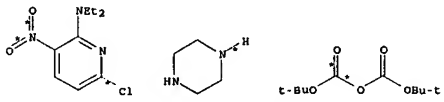
L9 ANSWER 19 OF 21 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 112:139649 CASREACT
TITLE: Novel 21-aminosteroids that inhibit iron-dependent lipid peroxidation and protect against central nervous system trauma
AUTHOR(S): Jacobsen, E. Jon; McCall, John M.; Ayer, Donald E.; VanDoornik, Fred J.; Palmer, John R.; Belonga, Kenneth L.; Braughler, J. Mark; Hall, Edward D.; Houser, David J.; et al.
CORPORATE SOURCE: CNS Res. Chem. Res. Prep., Upjohn Co., Kalamazoo, MI, 49001, USA
SOURCE: Journal of Medicinal Chemistry (1990), 33(4), 1145-51
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

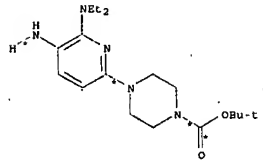
AB Twenty-two 21-amino steroids I [unsatd. = Δ4,9(11), Δ4, Δ9(11), Δ1,4, Δ1,4,9(11); R1 = H, β-OH, α-OH; R2 = H, Me; R3 = OH, H; R4 = H, Me; R5 = H, CH2CH2OH, 2-pyridyl, C6H4(OMe)-2, 6-methoxy-2-pyridyl, (3-hydroxy-2-pyridyl)methyl, 2,6-dipyrrolidino-4-pyrimidyl, etc.] were prepared Compds. within this series are potent inhibitors of iron-dependent lipid peroxidn. in rat brain homogenates with IC50 values as low as 3 μM. Furthermore, selected members enhance early neurol. recovery and survival in a mouse head injury model. Significant improvement in the 1 h post-head-injury neurol. status (grip test score) by as much as 168.6% of the control has been observed The most efficacious compound in this assay was I (unsatd. = Δ1,4,9(11), R1-R3 = H, R4 = Me, R5 = 2,6-dipyrrolidino-4-pyrimidyl) (II). II showed an increase in the 1-wk survival of 78.6% as compared to 27.3% for the vehicle-treated mice in the head-injury model.

RX(19) OF 27 COMPOSED OF RX(4), RX(5), RX(11)
RX(19) J + E + AM ===> S



J E AM

3
STEPS



S
YIELD 95%

RX(4) RCT J 125173-52-6, E 110-85-0
RGT K 584-08-7 K2CO3
PRO M 125173-54-8
SOL 75-05-8 MeCN

RX(5) RCT M 125173-54-8
RGT O 1333-74-0 H2, P 7647-01-0 HCl
PRO N 125173-55-9
CAT 7440-05-3 Pd
SOL 64-17-5 EtOH

RX(11) RCT N 125173-55-9, AM 24424-99-5
RGT AC 121-44-8 Et3N
PRO S 125173-56-0
SOL 75-09-2 CH2Cl2

L9 ANSWER 20 OF 21 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 98:54498 CASREACT
TITLE: Enkephalin derivatives
INVENTOR(S): Carr, Albert A.; Parr, Robert A.; Kane, John M.
PATENT ASSIGNEE(S): Richardson-Merrell Inc., USA
SOURCE: U.S., 25 pp. Cont.-in-part of U.S. Ser. No. 50,950, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4341698	A	19820727	US 1980-130431	19800314
ZA 8003338	A	19810527	ZA 1980-3338	19800604
CA 1161838	A1	19840207	CA 1980-353383	19800604
SE 8004254	A	19801222	SE 1980-4254	19800606
SE 447250	B	19861103		
SE 447250	C	19870212		
IL 60245	A	19850830	IL 1980-60245	19800606
IL 70788	A	19850830	IL 1980-70788	19800606
IL 70789	A	19850830	IL 1980-70789	19800606

DE 3022401	A1	19810108	DE 1980-3022401	19800614
CH 645363	A5	19840928	CH 1980-4698	19800617
CH 648835	A5	19850415	CH 1984-1248	19800617
GB 2051821	A	19810121	GB 1980-19903	19800618
GB 2051821	B	19830427		
ES 492566	A1	19810616	ES 1980-492566	19800618
AU 8059438	A	19810917	AU 1980-59438	19800619
AU 537042	B2	19840531		
BE 883943	A1	19801016	BE 1980-201125	19800620
DK 8002657	A	19801222	DK 1980-2657	19800620
NO 8001855	A	19801222	NO 1980-1855	19800620
NL 8003580	A	19801223	NL 1980-3580	19800620
FR 2459236	A1	19810109	FR 1980-13795	19800620
FR 2459236	B1	19840106		
JP 56007770	A	19810127	JP 1980-83006	19800620
JP 03031719	B	19910508		
FR 2473042	A1	19810710	FR 1981-2171	19810204
FR 2473042	B1	19830701		
US 4435571	A	19840306	US 1982-399553	19820719
US 4483988	A	19841120	US 1982-399554	19820719
GB 2106515	A	19830413	GB 1982-25842	19820910
GB 2132605	A	19840711	GB 1982-25828	19820910
GB 2132605	B	19850103		
AU 8291877	A	19830421	AU 1982-91877	19821224
CA 1179348	A2	19841211	CA 1983-441921	19831124
CA 1179349	A2	19841211	CA 1983-441922	19831124
SE 8500877	A	19850222	SE 1985-877	19850222
SE 460540	B	19891023		
SE 460540	C	19900215		
SE 460541	B	19891023	SE 1985-878	19850222
SE 460541	C	19900215		

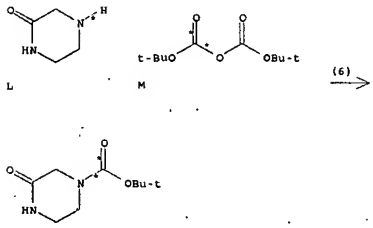
PRIORITY APPLN. INFO.:
US 1979-50950 19790621
US 1980-130431 19800314
CA 1980-353383 19800604
IL 1980-60245 19800606
CH 1980-4698 19800617
GB 1980-19903 19800618

OTHER SOURCE(S): MARPAT 98:54498
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Peptide derivs. I and II [R = H, OH, halo; R1 = H; R = R1 = OH; R2 = H, C1-4 alkyl; R3 = H, halo; R4 = H, C1-4 alkyl, CH(COR5)CH2CHMe2 or CH(COR5)CH2CH2SMe (R5 = OH, NH2, alkylamino, dialkylamino); Z = CH2, CO, CH(OH), S, SO, SO2] were prepared as analgesics and antipsychotics (no data). Thus, piperazinone III (Boc = Me3CO2C) was benzylated with p-(PhCH2O)C6H4CH2Cl in THF/hexane containing BuLi and (Me2CH)2NH to give 53% piperazine IV (R6 = H), which was treated with BrCH2CO2Me in THF containing NaH to give 74% IV (R6 = CH2CO2Me), which was saponified by aqueous LiOH to give IV (R6 = CH2CO2H). The latter was condensed with H-Gly-Phe-NHMe.HCl by ClCO2CH2CHMe2 in THF containing Et3N to give peptide V (R7 = PhCH2, R8 = Boc), which underwent hydrogenolysis to give V (R7 = H, R8 = Boc), which was Boc-deblocked by CF3CO2H to give V (R7 = R8 = H).

RX(6) OF 29 L + M ===> A...



L M A

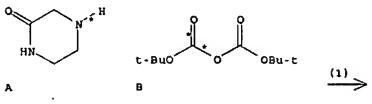
RX(6) RCT L 5625-67-2, M 24424-99-5
PRO A 76003-29-7

L9 ANSWER 21 OF 21 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 94:15672 CASREACT
TITLE: Alkylation of protected piperazinone dianions
AUTHOR(S): Kane, John M.; Carr, Albert A.
CORPORATE SOURCE: Merrell Res. Cent., Cincinnati, OH, 45215, USA
SOURCE: Tetrahedron Letters (1980), 21(32), 3019-20
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

I

AB Piperazinones I (R = CO2CMe3, R1 = Me, CH2Ph, CH2C6H4OCH2Ph-4, R2 = R3 = H) were prepared (39-79%) from I (R-R3 = H) by sequential protection with (Me3CO2C)2O, metalation with LiN(CHMe2)2, and alkylation of the resulting dianion. The prepns. of I (R = CO2CMe3)(R1 = SPh, R2 = R3 = H; R1R2 = CHPh, R3 = H; R1 = CH2C6H4OCH2Ph-4, R2 = H, R3 = CH2CO2Me; R1 = CH2C6H4OCH2Ph-4, R2 = R3 = Me) are also reported.

RX(1) OF 14 A + B ===> C...



A B C

RX(1) RCT A 5625-67-2, B 24424-99-5
PRO C 76003-29-7

=> d his

(FILE 'HOME' ENTERED AT 17:11:43 ON 24 JUL 2007)

FILE 'REGISTRY' ENTERED AT 17:11:49 ON 24 JUL 2007
L1 STRUCTURE UPLOADED

FILE 'REGISTRY' ENTERED AT 17:12:55 ON 24 JUL 2007
L2 STRUCTURE UPLOADED

FILE 'CASREACT' ENTERED AT 17:13:29 ON 24 JUL 2007
L3 5 S L2
L4 128 S L2 FULL
L5 STRUCTURE UPLOADED
L6 4 S L5
L7 63 S L5 FULL

FILE 'CASREACT' ENTERED AT 17:20:23 ON 24 JUL 2007
L8 63 S L7 FULL
L9 21 S L8 AND PY<2003